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Trans-Fats and Coronary Heart Disease

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A large body of data from epidemiologic, clinical trial, animal, and in vitro studies demonstrate adverse consequences of industrially synthesized trans fatty acids (TFAs) on the risk of coronary heart disease (CHD). A growing database of more recent research from virtually all experimental models demonstrates evidence of detrimental consequences of TFAs on the risk of diabetes. Evidence is accumulating about the physiological and cellular mechanisms of action that account for the many adverse effects TFAs have on CHD and diabetes. In a relatively short period of time (i.e., from around the early 1990s to the present time, or almost 20 years), we have gained a good understanding of the health effects of TFAs from epidemiologic studies, clinical trials/studies, animal research, and in vitro experiments that collectively justify current dietary recommendations made by numerous government agencies and health organizations to consume a diet with as little TFAs as possible. Public policy actions have been implemented and TFAs appear on the Nutrition Facts Panel. Some cities have also mandated zero TFAs in restaurants. The research on TFAs is a good example of how an evidence base has been built and translated into public policy that targets improved health. It is impressive that the TFA research has been coupled to public policy actions to decrease TFAs in the food supply so quickly.

A seminal paper published by Mensink and Katan (1990) reported that a diet with 10% of energy from TFAs versus a diet with 10% of energy from oleic acid significantly ($P < 0.001$) increased LDL cholesterol (LDL-C) (14 mg/dL) and significantly lowered ($P < 0.001$) HDL cholesterol (HDL-C) (7 mg/dL). Saturated fat (10% of energy) also increased LDL-C (18 mg/dL), but had no effect on HDL-C compared with oleic acid. The authors concluded that the effect of TFAs on the serum lipoprotein profile is at least as unfavorable as that of the cholesterol-raising saturated fatty acids (SFAs) because of their similar LDL-C raising effects. Moreover, TFAs may be more detrimental because they also lower HDL-C versus SFAs. Soon after, Willett and colleagues (1993) published the results from the Nurses' Health Study of 85,095 women without diagnosed CHD, stroke, diabetes, or hypercholesterolemia at the start of the study, and reported that the intake of TFA isomers was related to the risk of CHD after 8 years of follow-up. Using the Willett food frequency questionnaire, the authors reported that TFAs increased relative risk (highest versus lowest quintile was 1.50 [95% confidence interval: 1.12–2.00], P for trend = 0.001). The authors concluded that the consumption of partially hydrogenated vegetable oils may contribute to occurrence of CHD.

In an early review evaluating the scientific evidence on TFAs and CHD (Allison et al., 1995), data supporting a relation between TFA intake and CHD risk were considered equivocal on the basis of results reported from observational studies that had methodological limitations, and animal studies that showed no differences in LDL-C and atherosclerosis incidence in response to diets high in TFAs. The authors called for additional research to resolve questions about the independent effects of TFAs on plasma lipoproteins and their mechanisms of action. In a position paper on TFAs published by the American Society of Clinical Nutrition (ASCN)/American Institute of Nutrition (AIN) Task Force on Trans Fatty Acids (1996), the authors noted, based on the state of the science to date, that it cannot be concluded that the intake of TFAs is a risk factor for CHD. The position paper noted that there were few rigorous studies that addressed the biomedical effects of TFAs and possible mechanisms relevant to human health and disease. Before making any new dietary recommendations or changes in nutrition policy concerning TFAs, the position paper concluded that data were needed, comparable to that available for SFAs, about the intake of TFAs, their biological effects and associated mechanisms of action, and their relation to disease. Based on the current database available at the time of its publication, the ASCN/AIN position paper on TFAs concluded that it was premature to make new dietary recommendations for the population at large or to change nutrition policy with respect to TFA labeling. The "early" consensus was that the "debate" about TFAs should not detract from the role that SFAs played in CHD risk.

Over the next decade, additional epidemiologic studies were published that showed a consistent adverse association of TFAs with increased CHD risk (reviewed by Mozaffarian et al., 2006). In addition, well-controlled, clinical studies were conducted that showed a dose-response relationship between dietary TFAs and LDL-C (Judd et al., 2002; Lichtenstein et al., 1999). Collectively, the clinical studies demonstrated a dose-response relationship between TFA intake and TC/HDL-C (reviewed by Ascherio et al., 1999). Meta-analyses evaluated the effects of substituting TFAs for carbohydrate calories and demonstrated an LDL-C raising effect that was similar to SFAs; however, unlike SFAs, TFAs did not raise HDL-C (Mensink et al., 2003), resulting in the conclusion that TFAs lower HDL-C compared to SFAs and consequently increase the LDL-C/HDL-C ratio, which is a strong independent risk factor for CVD.

In a relatively short period of time, there has been an impressive evolvement of the evidence base demonstrating an adverse relationship between TFA intake and CHD risk. The epidemiologic studies were instrumental in establishing the rationale for conducting well-controlled clinical studies that definitively demonstrated the role that TFA intake played in CHD risk. The proliferation of the evidence base was key for the current actions/policies that have been implemented to decrease TFAs in the food supply. The emerging data or TFA intake and diabetes incidence (Riserus et al., 2009) insulin resistance and adiposity (Teegala et al., 2009) could reinforce the importance of decreasing TFAs in the diet. It will be interesting to see how this story will unfold. Other emerging questions about TFAs to resolve include determining the effects of animal TFAs versus industrially synthesized TFAs (Willett and Mozaffarian, 2008) and the biological effects of the individual industrially synthesized TFA (Lemaitre et al., 2006). Nonetheless, it is beyond debate that removing industrially produced TFAs from the diet will decrease risk of chronic disease(s) such as CHD and, possibly, diabetes.

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